Preparation for Term Paper (Genomic Heritability Calculations)

Review from <u>Barry et al. 2023</u> (*Figure 1*)

Family Based Designs

- Twin Studies
- Extended Twin Design (including other relatives)

Genomic Methods: Unrelated Individuals

- Linkage Disequilibrium (LD) Score Regression
 - Supplemental Materials describe implementation in <u>LDSC</u> package (<u>Bulik-Sullivan et al. 2015</u>).
- Genomic relatedness REstricted Maximum-Likelihood (GREML)
 - Part of GCTA (Genome-wide Complex Trait Analysis, Yang et al. 2011)
 - GCTA Wikipedia Entry
- LD- and MAF-stratified GREML (GREML-LDMS, Yang et al. 2015)

• Genomic Methods: Related Individuals

- GREML-KIN (GREML with KINship analysis Hill et al. 2018, Xia et al. 2016, and/or Zaitlen et al. 2013.
 - On the GCTA website, the section for "GREML in family data" references Zaitlen et al. 2013.
- Trio-GCTA (Eilertsen et al. 2021)
- Material (or Paternal) GCTA (M-GCTA, Qiao et al. 2020)
- Relatedness Disequilibrium Regression (RDR, Young et al. 2018)
 - Supplemental Materials also reference Visscher et al. 2006.
- Table 1 also describes strengths and limitations, which include the relative estimated contribution of rare variants.
- Box 1 defines narrow-sense heritability versus broad sense heritability.

Methods for *Unrelated* Individuals

• Genomic relatedness REstricted Maximum-Likelihood (*GREML*)

Methods Considering *Related* Individuals

• Relatedness Disequilibrium Regression (RDR, Young et al. 2018)

Additional Reviews (referenced by <u>Barry et al. 2023</u>)

- In addition to the <u>Visscher et al. 2010</u> height GWAS article mentioned in the <u>Height QTL Notes</u>, <u>Barry et al. 2023</u> reference a review related to heritability and genomics in <u>Visscher et al. 2008</u>.
- A review by <u>Mayhew et al. 2017</u> is also referenced.
- <u>Yang et al. 2017</u> includes a figure related to estimation of height heritability with *different methods*.
- Young 2019 includes a table showing variation in heritability values for height (with *different methods* and in different cohorts).
- Zhu and Zhou 2020 is another cited review.

Previous Related Discussions

- I have a *journal comment/question* for <u>Young 2019</u>, which was referenced in the <u>Barry et al. 2023</u> review.
- I have a *preprint comment* for <u>Dolan et al. 2019</u>, which specifically references *RDR* (in reference to *Young 2019* comment/question above) as well as *heritability*.
- I have preprint comment on an article titled "Recovery of trait heritability from whole genome sequence data" (with a later peer-reviewed version published in Wainschtein et al. 2022).
- As might be expected, "heritability" is mentioned in the earlier preprint comment for the Bloom et al. 2019 data that I am (partially) re-analyzing.
- Because data analysis was not performed, it may be somewhat off topic. However, there was mention to interpretation of heritability in a *preprint comment* on <u>Lowes et al. 2022</u>.
- While not exactly about heritability, I have a *preprint comment* related to predicting height for Thompson et al. 2022.
- Height is also briefly mentioned in a <u>Disgus</u> comment for <u>Marnetto et al. 2020</u>, even if not currently visible on the journal website?.

Newer/Additional Methods

- GPLEMMA (Kerin and Marchini 2020)
 - Cites RDR publication (Young et al. 2018)
- SAFE-h² (Darbani and Nicolaisen 2023)
 - Includes comparisons to EMMAX (Kang et al. 2010) and LDAK.
 - EMMAX = EMMA eXpeditated, an extension of EMMA (Kang et al. 2008).
 - Two implementations for LDAK are mentioned. One is within GCTA, and the other is described as LDAK-Thin (Speed et al. 2012).
- The GCTA webpage lists sBLUP among available methods, but not necessarily for heritability?
 - sBLUP = Summary-level BLUP
 - Best Linear Unbiased Prediction (<u>BLUP</u>) is referenced in <u>Wang et al. 2019</u>
 - The *rrBLUP* (ridge-regression BLUP) R-package is a <u>dependency</u> for the *Bloom et al. 2019* code (imported in <u>mapping.R</u>, for example).
- While not an additional method, Tang et al. 2022 is an additional review on the general topic.
 - Includes descriptions of additional methods.
- <u>Srivastava et al. 2023</u> is another such review.
 - Describes <u>REML</u> (REstricted Maximum Likelihood, with applications in <u>Lee et al. 2006</u> and <u>Yang et al. 2010</u>) for individual-level data, before listing assumptions for <u>GREML</u> versus <u>LDAK</u>.
- Bloom et al. 2019 references de los Campos et al. 2015 ("Genomic Heritability: What Is It?")
- Evans et al. 2018 provides a comparison of different methods.
 - It looks like there is noticeable emphasis on implementation of GREML and LDAK methods.